Docket No.: PF-0475-2 DIV

Response Under 37 C.F.R. 1.116 - Expedited Procedure
Examining Group 1644

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of: Lal et al.

Title: HUMAN SHORT-CHAIN DEHYDROGENASE

Serial No.: 10/006,163 Filing Date: December 4, 2001

Examiner: Huynh, P.N. Group Art Unit: 1644

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Sir:

Further to the Notice of Appeal filed May 7, 2003, and received at the Patent Office on May 12, 2003, herewith are three copies of Appellants' Brief on Appeal. Authorized fees include the $320 fee for the filing of this Brief.

This is an appeal from the decision of the Examiner finally rejecting claims 11, 31, 32, 34, 36-43, and 58 of the above-identified application.

(1) REAL PARTY IN INTEREST

The above-identified application is assigned of record to Incyte Pharmaceuticals, Inc. (now Incyte Corporation), (Reel 9324, Frame 0338) who is the real party in interest herein.

(2) RELATED APPEALS AND INTERFERENCES

Appellants, their legal representative and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

(3) STATUS OF THE CLAIMS

Claims rejected:	Claims 11, 31, 32, 34, 36-43, and 58
Claims allowed:	none
Claims canceled:	Claims 2-10, 12-29, 46-55, and 57
Claims withdrawn:	Claims 1, 30, 33, 35, 44, 45, and 56
Claims on Appeal:	Claims 11, 31, 32, 34, 36-43, and 58 (A copy of the claims on appeal, as amended by the Amendment After Final filed concurrently with this Brief, can be found in the attached Appendix.)

(4) STATUS OF AMENDMENTS AFTER FINAL

An Amendment after Final Rejection under 37 C.F.R. § 1.116 is filed concurrently herewith. This Amendment removes issues for appeal. Therefore, it is believed that this Amendment will be entered.

(5) SUMMARY OF THE INVENTION

Appellants' invention is directed to antibodies which specifically bind to polypeptides, including short-chain dehydrogenase HSCD, comprising the amino acid sequence of SEQ ID NO:1 (Specification, e.g., at page 3, lines 2-4; page 4, lines 9-11; page 14, lines 22-24; page 15, lines 1-2; and page 28, lines 7-12). Appellants' invention also includes antibodies which specifically bind to polypeptides at least 90% identical to SEQ ID NO:1 (e.g., at page 3, lines 5-6), or to polypeptides which comprise fragments of SEQ ID NO:1 (e.g., at page 3, lines 2-7; page 4, lines 9-11; and page 28, lines 25-27). The invention further includes compositions comprising the foregoing antibodies (e.g.,

at page 32, lines 13-16), and methods of making the foregoing antibodies (e.g., at page 28, line 6 to page 29, line 17; and page 51, lines 4-19).

HSCD has strong chemical and structural homology with short-chain acyl CoA dehydrogenase (GenBank ID 2315796; SEQ ID NO:3) (Specification, e.g., at page 15, lines 7-8). In particular, HSCD and short-chain acyl CoA dehydrogenase share 43% identity (e.g., at page 15, lines 8-9; and Figure 2). In addition:

> "HSCD is 313 amino acids in length and has four potential casein kinase II phosphorylation sites at residues S_{65}, T_{73}, S_{114}, and S_{224}; one potential glycosaminoglycan attachment site at residue S_{286}; one potential microbodies C-terminal targeting signal site at residue S_{311}; four potential N-myristoylation sites at residues G_{14}, G_{18}, G_{164}, and G_{194}; and five potential protein kinase C phosphorylation sites at residues T_{37}, T_{43}, S_{232}, S_{249}, and T_{310}. . . HSCD and short-chain acyl-CoA dehydrogenase share 43% identity, the N-myristoylation sites at residues G_{14} and G_{18}, and the protein kinase C phosphorylation sites at residues T_{37} and S_{249}. . . Northern analysis shows the expression of this sequence in various libraries, at least 50% of which are immortalized or cancerous and at least 27% of which involve the immune response. Of particular note is the expression of HSCD in reproductive tissue libraries." (Specification at page 15, lines 2-14)

The antibodies of the present invention are useful, for example, for purifying and detecting polypeptides which have specific uses in toxicology testing, drug discovery, and disease diagnosis (Specification, e.g., at page 25, lines 4-11; page 35, line 29 to page 36, line 17; and page 41, lines 20-23).

(6) ISSUES

1. Whether claims 11, 36, and 37 are anticipated under 35 U.S.C. § 102(b) by Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857).

2. Whether claims 11, 31, 42, and 43 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Queen et al. (U.S. Patent No. 6,180,370 B1).

3. Whether claims 11 and 31 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Ladner et al. (U.S. Patent No. 4,946,778).

4. Whether claims 11, 31, 32, and 34 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Harlow et al. (in Antibodies a Laboratory Manual, 1988, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pages 319-356 and 626-629).

5. Whether claims 11 and 38-41 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Harlow et al. (in Antibodies a Laboratory Manual, 1988, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pages 139-149).

6. Whether claims 11, 31, 32, 34, 36-43, and 58 meet the enablement requirement of 35 U.S.C. § 112, first paragraph.

7. Whether claims 11, 31, 32, 34, 36-43, and 58 meet the written description requirement of 35 U.S.C. § 112, first paragraph.

(7) GROUPING OF THE CLAIMS

As to Issue 1

Claims 11, 36, and 37 are grouped together.

As to Issue 2

Claims 11, 31, 42, and 43 are grouped together.

As to Issue 3

Claims 11 and 31 are grouped together.

As to Issue 4

Claims 11, 31, 32, and 34 are grouped together.

As to Issue 5

Claims 11 and 38-41 are grouped together.

As to Issue 6

All of the claims on appeal are grouped together.

As to Issue 7

All of the claims on appeal are grouped together.

(8) APPELLANTS' ARGUMENTS

Issue 1 – Whether claims 11, 36, and 37 are anticipated under 35 U.S.C. § 102(b) by Verwoert et al.

Claims 11, 36, and 37 were rejected under 35 U.S.C. § 102(b) because the recited antibodies are allegedly anticipated by Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857). This rejection is traversed.

The Examiner asserts that "Verwoert *et al* teach an antibody that binds to a fragment such as VTGASRGIGRGIA of a polypeptide such as Malonyl coenzyme A-Acyl carrier protein transacylase that has a stretch of contiguous amino acid residues identical to the claimed SEQ ID NO:1" (Office Action, February 11, 2003; page 2 at § 6). This is incorrect. While it may be true that the antibodies taught by Verwoert et al. could possibly bind to a polypeptide comprising SEQ ID NO:1, or fragments or variants thereof, this binding would not be **specific**. For example, the specification discloses that:

> Various immunoassays may be used for screening to identify antibodies having the **desired specificity**. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between HSCD and its **specific antibody**. (Specification, page 29, lines 24-28; emphasis added)

The antibodies recited by the claims **specifically** bind to a polypeptide comprising SEQ ID NO:1, or fragments or variants thereof. The antibodies taught by Verwoert et al. are excluded from the claimed antibodies because they bind to polypeptides other than those recited in the claims.

Appellants do not concede to the Examiner's assertions. However, to expedite prosecution by removing issues for appeal, claim 11 has been amended by the Amendment filed concurrently herewith.

Therefore, this rejection of claims 11, 36, and 37 should be overturned.

Issue 2 – Whether claims 11, 31, 42, and 43 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. in view of U.S. Patent No. 6,180,370 B1

Claims 11, 31, 42, and 43 were rejected under 35 U.S.C. § 103(a) because the claimed antibodies are allegedly obvious over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Queen et al. (U.S. Patent No. 6,180,370 B1). This rejection is traversed.

This rejection is based on the allegation that the antibodies taught by Verwoert et al. are within the scope of the claimed antibodies. As discussed above under Issue 1, the claims recite antibodies which **specifically** bind to a polypeptide comprising SEQ ID NO:1, or fragments or variants thereof. The antibodies taught by Verwoert et al. are excluded from the claimed antibodies because they bind to polypeptides other than those recited in the claims.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." M.P.E.P. § 2143.03. In addition, "the reference teachings must somehow be modified in order to meet the claims. The modification must be one which would have been obvious to one of ordinary skill in the art at the time the invention was made." M.P.E.P. § 706.02. Since the claim language distinguishes the recited antibodies from the antibodies taught by Verwoert et al., the Examiner has not convincingly shown how the teachings of Verwoert et al. and/or Queen et al. could be modified in order to arrive at the claimed subject matter. Therefore, the Examiner has not met the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103.

Appellants do not concede to the Examiner's assertions. However, to expedite prosecution by removing issues for appeal, claim 11 has been amended by the Amendment filed concurrently herewith.

Therefore, this rejection of claims 11, 31, 42, and 43 should be overturned.

Issue 3 – Whether claims 11 and 31 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. in view of U.S. Patent No. 4,946,778

Claims 11 and 31 were rejected under 35 U.S.C. § 103(a) because the claimed antibodies are allegedly obvious over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Ladner et al. (U.S. Patent No. 4,946,778). This rejection is traversed.

This rejection is based on the allegation that the antibodies taught by Verwoert et al. are within the scope of the claimed antibodies. As discussed above under Issue 1, the claims recite antibodies which **specifically** bind to a polypeptide comprising SEQ ID NO:1, or fragments or variants thereof. The antibodies taught by Verwoert et al. are excluded from the claimed antibodies because they bind to polypeptides other than those recited in the claims.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." M.P.E.P. § 2143.03. In addition, "the reference teachings must somehow be modified in order to meet the claims. The modification must be one which would have been obvious to one of ordinary skill in the art at the time the invention was made." M.P.E.P. § 706.02. Since the claim language distinguishes the recited antibodies from the antibodies taught by Verwoert et al., the Examiner has not convincingly shown how the teachings of Verwoert et al. and/or Ladner et al. could be modified in order to arrive at the claimed subject matter. Therefore, the Examiner has not met the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103.

Appellants do not concede to the Examiner's assertions. However, to expedite prosecution by removing issues for appeal, claim 11 has been amended by the Amendment filed concurrently herewith.

Therefore, this rejection of claims 11 and 31 should be overturned.

Issue 4 – Whether claims 11, 31, 32, and 34 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. in view of Harlow et al. (pages 319-356 and 626-629)

Claims 11, 31, 32, and 34 were rejected under 35 U.S.C. § 103(a) because the claimed antibodies are allegedly obvious over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of

Harlow et al. (in Antibodies a Laboratory Manual, 1988, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pages 319-356 and 626-629). This rejection is traversed.

This rejection is based on the allegation that the antibodies taught by Verwoert et al. are within the scope of the claimed antibodies. As discussed above under Issue 1, the claims recite antibodies which **specifically** bind to a polypeptide comprising SEQ ID NO:1, or fragments or variants thereof. The antibodies taught by Verwoert et al. are excluded from the claimed antibodies because they bind to polypeptides other than those recited in the claims.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." M.P.E.P. § 2143.03. In addition, "the reference teachings must somehow be modified in order to meet the claims. The modification must be one which would have been obvious to one of ordinary skill in the art at the time the invention was made." M.P.E.P. § 706.02. Since the claim language distinguishes the recited antibodies from the antibodies taught by Verwoert et al., the Examiner has not convincingly shown how the teachings of Verwoert et al. and/or Harlow et al. (pages 319-356 and 626-629) could be modified in order to arrive at the claimed subject matter. Therefore, the Examiner has not met the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103.

Appellants do not concede to the Examiner's assertions. However, to expedite prosecution by removing issues for appeal, claim 11 has been amended by the Amendment filed concurrently herewith.

Therefore, this rejection of claims 11, 31, 32, and 34 should be overturned.

Issue 5 – Whether claims 11 and 38-41 are obvious under 35 U.S.C. § 103(a) over Verwoert et al. in view of Harlow et al. (pages 139-149)

Claims 11 and 38-41 were rejected under 35 U.S.C. § 103(a) because the claimed antibodies are allegedly obvious over Verwoert et al. (J. Bacteriol., 1992, 174:2851-2857) in view of Harlow et al. (in Antibodies a Laboratory Manual, 1988, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pages 139-149). This rejection is traversed.

This rejection is based on the allegation that the antibodies taught by Verwoert et al. are within the scope of the claimed antibodies. As discussed above under Issue 1, the claims recite antibodies

which **specifically** bind to a polypeptide comprising SEQ ID NO:1, or fragments or variants thereof. The antibodies taught by Verwoert et al. are excluded from the claimed antibodies because they bind to polypeptides other than those recited in the claims.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." M.P.E.P. § 2143.03. In addition, "the reference teachings must somehow be modified in order to meet the claims. The modification must be one which would have been obvious to one of ordinary skill in the art at the time the invention was made." M.P.E.P. § 706.02. Since the claim language distinguishes the recited antibodies from the antibodies taught by Verwoert et al., the Examiner has not convincingly shown how the teachings of Verwoert et al. and/or Harlow et al. (pages 139-149) could be modified in order to arrive at the claimed subject matter. Therefore, the Examiner has not met the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103.

Appellants do not concede to the Examiner's assertions. However, to expedite prosecution by removing issues for appeal, claim 11 has been amended by the Amendment filed concurrently herewith.

Therefore, this rejection of claims 11 and 38-41 should be overturned.

Issue 6 – Whether claims 11, 31, 32, 34, 36-43, and 58 meet the enablement requirement of 35 U.S.C. § 112, first paragraph

Claims 11, 31, 32, 34, 36-43, and 58 stand rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the specification does not describe the subject matter of the invention in such a way as to enable one of skill in the art to make and/or use antibodies which specifically bind to the recited "variants" and "fragments" of SEQ ID NO:1. In particular, the Examiner asserts that the specification "**does not** reasonably provide enablement for (1) *any* isolated antibody . . . which specifically binds to *any* polypeptide 'comprising' any fragment of a polypeptide consisting of the amino acid sequence of SEQ ID NO:1, wherein the antibody specifically binds to *any* epitope of the fragment of a polypeptide of SEQ ID NO:1, . . . which specifically binds to any polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, wherein said polypeptide has CoA dehydrogenase activity, and wherein the antibody specifically

binds to *any* epitope of the fragment of a polypeptide at least 90% identical to SEQ ID NO:1, . . . [or] which specifically binds to a polypeptide 'comprising' any 'fragment' of a polypeptide, such as any fragment 'comprises' at least 15 contiguous amino acid residues of SEQ ID NO:1 . . ." (Office Action, February 11, 2003; pages 12-13; emphasis in original). Such, however, is not the case.

The specification discloses methods to make antibodies which specifically bind to a polypeptide having **any** particular amino acid sequence (e.g., at page 28, line 6 to page 29, line 23; and page 51, lines 4-19). Given the information provided by SEQ ID NO:1 (the amino acid sequence of HSCD), one of skill in the art would be able to routinely obtain antibodies which specifically bind to any of the recited polypeptides, variants, and fragments of SEQ ID NO:1, including "an antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1, wherein the antibody specifically binds to an epitope of a polypeptide of SEQ ID NO:1," "an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, wherein said polypeptide has CoA dehydrogenase activity, and wherein the antibody specifically binds to an epitope of a polypeptide at least 90% identical to SEQ ID NO:1," and "an antibody which specifically binds to a polypeptide comprising an immunogenic fragment of a polypeptide consisting of the amino acid sequence of SEQ ID NO:1, wherein said fragment comprises at least 15 contiguous amino acid residues of SEQ ID NO:1, and wherein the antibody specifically binds to an epitope of the fragment." For example, an animal could be immunized with any of the recited polypeptides, variants, and fragments of SEQ ID NO:1, antibodies could be isolated from the animal, and the antibodies could be screened to identify antibodies which specifically bind to the polypeptide, variant, or fragment.

Likewise, the specification discloses methods to use antibodies which specifically bind to a polypeptide having **any** particular amino acid sequence in, for example, the purification of such polypeptides (e.g., at page 51, line 21 to page 52, line 2), the detection and/or measurement of such polypeptides (e.g., at page 25, lines 4-11; and page 35, line 29 to page 36, line 17), and the competitive screening of drug candidates (e.g., at page 41, lines 20-23). Given the information provided by SEQ ID NO:1 (the amino acid sequence of HSCD), one of skill in the art would be able to routinely use antibodies which specifically bind to any of the recited polypeptides, variants, and

fragments of SEQ ID NO:1, including "an antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1, wherein the antibody specifically binds to an epitope of a polypeptide of SEQ ID NO:1," "an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, wherein said polypeptide has CoA dehydrogenase activity, and wherein the antibody specifically binds to an epitope of a polypeptide at least 90% identical to SEQ ID NO:1," and "an antibody which specifically binds to a polypeptide comprising an immunogenic fragment of a polypeptide consisting of the amino acid sequence of SEQ ID NO:1, wherein said fragment comprises at least 15 contiguous amino acid residues of SEQ ID NO:1, and wherein the antibody specifically binds to an epitope of the fragment." For example, an antibody which specifically binds to any of the recited polypeptides, variants, and fragments of SEQ ID NO:1 could be coupled to an activated chromatographic resin, and this resin could then be used in an immunoaffinity column to purify the polypeptide, variant, or fragment.

The Examiner assails the use of the term "comprising" by stating that "the term 'comprising' is open-ended. It expands the polypeptide fragment to which the antibody binds to include additional amino acids at either or both ends. There is insufficient guidance as to the binding specificity of the claimed antibody and the immunogen used by applicant to generate antibody that would bind specifically not only to SEQ ID NO:1, but also to a polypeptide having undisclosed amino acids at either or both ends" (Office Action, February 11, 2003; page 14). To the contrary, the claimed antibodies are fully enabled by the specification.

The Examiner's assertions seem to imply that the use of the transitional phrase "comprising" in claim 11 requires that the specification provide enablement for any possible element which could be a part of, but is not essential to, the claimed subject matter. However, the transitional phrase " '[c]omprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." M.P.E.P. § 2111.03 (citing *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997)). The specification has disclosed numerous examples of polypeptides

"comprising" the recited polypeptides, variants, and fragments of SEQ ID NO:1, such as fusion proteins and coupled proteins (Specification, e.g., at page 7, lines 24-29; page 19, lines 26-28; page 26, lines 2-15; page 28, lines 25-27; and page 51, lines 13-19). One of skill in the art would understand how to make and use antibodies which specifically bind to the disclosed polypeptides, "comprising" the recited polypeptides, variants, and fragments of SEQ ID NO:1, without an explicit disclosure of every possible element which could be a part of, but is not essential to, the claimed subject matter.

Moreover, the claims recite antibodies which specifically bind to epitopes on the recited polypeptides, variants, and fragments of SEQ ID NO:1. For example, the claimed antibodies specifically bind to "an epitope of a polypeptide of SEQ ID NO:1," "an epitope of a polypeptide at least 90% identical to SEQ ID NO:1," and "an epitope of the fragment [of SEQ ID NO:1]." Since the claimed antibodies specifically bind to the recited epitopes, and since a skilled artisan would know how to make and use antibodies which specifically bind to epitopes of the recited polypeptides, variants, and fragments of SEQ ID NO:1, any additional amino acid residues at "either or both ends" of the recited polypeptides, variants and fragments of SEQ ID NO:1 are not essential to the claimed subject matter. Therefore, it is irrelevant whether the specification enables antibodies which specifically bind to additional amino acid residues at "either or both ends" of the recited polypeptides, variants, and fragments of SEQ ID NO:1.

The Examiner states that "[w]ith regard to antibody that binds to a polypeptide having only 90% identity to SEQ ID NO:1, . . . [t]he specification does not provide guidance as to which one or more amino acids of SEQ ID NO:1 is altered such as substitution, insertion and deletion and whether the resulting polypeptide variant has biological function" (Office Action, February 11, 2003; page 14). This is irrelevant. Antibodies which specifically bind to a polypeptide can be made as long as that polypeptide, or fragments thereof, are available; there is no restriction on the amino acid sequence of polypeptides that can be used to make antibodies. Since a polypeptide having **any** amino acid sequence (including any amino acid sequence that is at least 90% identical to SEQ ID NO:1 and any naturally occurring amino acid sequence that is at least 90% identical to SEQ ID NO:1) can be used to

make antibodies using the methods disclosed in the specification, it is not necessary to identify particular naturally occurring amino acid sequences that are at least 90% identical to SEQ ID NO:1 that could be used in this manner. Moreover, the question of whether a "polypeptide variant has biological function" is irrelevant to the enablement of antibodies which specifically bind to that polypeptide variant. Even if a polypeptide variant has no known biological function, it can nevertheless be used to make antibodies which specifically bind to that polypeptide variant, without undue experimentation.

In support of this rejection, the Examiner states that "[i]n the absence of guidance as to the specific amino acid residues (the antigenic determinant) used by applicant for immunization and the specific epitope of SEQ ID NO:1, or fragment thereof to which the antibody binds, it is unpredictable which antibody generated from the full length polypeptide of SEQ ID NO:1 would bind specifically to an undisclosed polypeptide having addition, deletion, and insertion or fragment of SEQ ID NO:1" (Office Action, February 11, 2003; pages 14-15). However, it is not necessary to predict "which antibody generated from the full length polypeptide of SEQ ID NO:1 would bind specifically to an undisclosed polypeptide having addition, deletion, and insertion or fragment of SEQ ID NO:1." All that is necessary to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, is that a skilled artisan would reasonably understand how to make and use the claimed antibodies, without undue experimentation.

Antibodies which specifically bind to a polypeptide can be made as long as that polypeptide, or fragments thereof, are available; there is no restriction on the amino acid sequence of polypeptides that can be used to make antibodies. Thus, any of the recited polypeptides (including polypeptides having an amino acid sequence that is at least 90% identical to SEQ ID NO:1, a naturally occurring amino acid sequence that is at least 90% identical to SEQ ID NO:1, or an amino acid sequence that is a fragment of SEQ ID NO:1) can be used to make antibodies using the methods disclosed in the specification. A skilled artisan would be able to routinely determine whether a given antibody produced in this way specifically binds to the polypeptide used to make that antibody, without undue experimentation. For example, an antibody can be subjected to a screen which identifies antibodies that specifically bind to the polypeptide.

Citing Kuby et al. (Immunology, Second edition, 1994, W.H. Freeman and Company, New York, NY, pages 86-96), the Examiner states that "[e]ven if the fragment is limited to consisting of 15 contiguous amino acid residues of SEQ ID NO:1, the antibody generated from said fragment may not bind to the full-length polypeptide of SEQ ID NO:1 as taught by Kuby et al." (Office Action, February 11, 2003; page 15). In making this statement, the Examiner has improperly imported additional limitations into the claims. In making an antibody which specifically binds to the full-length polypeptide of SEQ ID NO:1, there is no requirement to use a fragment consisting of 15 contiguous amino acid residues of SEQ ID NO:1. In fact, there is no requirement that **any particular polypeptide** be used to make any of the claimed antibodies. The claims recite antibodies which specifically bind to the recited polypeptides, variants, and fragments of SEQ ID NO:1. All that is necessary to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, is that a skilled artisan would reasonably understand how to make and use the claimed antibodies, without undue experimentation.

As stated above, antibodies which specifically bind to a polypeptide can be made as long as that polypeptide, or fragments thereof, are available; there is no restriction on the amino acid sequence of polypeptides that can be used to make antibodies. Thus, the full-length polypeptide of SEQ ID NO:1 can be used to make antibodies using the methods disclosed in the specification. A skilled artisan would be able to routinely determine whether a given antibody produced in this way specifically binds to the full-length polypeptide of SEQ ID NO:1, without undue experimentation. For example, an antibody can be subjected to a screen which identifies antibodies that specifically bind to the full-length polypeptide of SEQ ID NO:1.

The Examiner attempts to provide further support for this rejection by citing Ngo et al. (in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Birkhauser Boston, pages 492-495) and Abaza et al. (J. Prot. Chem., 1992, 11:433-444). The Examiner asserts that "Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance" (Office Action, February 11, 2003; page 15). Once again, the question is not whether the recited polypeptides which are specifically bound by the claimed antibodies retain the structure and/or function of the SEQ ID NO:1 polypeptide. The relevant question, for the

purposes of enablement under 35 U.S.C. § 112, first paragraph, is whether a skilled artisan could make and use the claimed antibodies which specifically bind the recited polypeptides. Regardless of whether a variant or fragment of SEQ ID NO:1 maintains the structure and/or function of the SEQ ID NO:1 polypeptide, that variant or fragment could still be used to make antibodies, without undue experimentation. Thus, the enablement requirement is satisfied.

With respect to the Abaza reference, the Examiner contends that "even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity (binding) of a protein with monoclonal antibody against the site" (Office Action, February 11, 2003; page 17). However, whether or not the Examiner's contention is true, it has no bearing on whether one of skill in the art could make and/or use the claimed antibodies, without undue experimentation. Even if a polypeptide variant has an amino acid substitution which drastically affects the reactivity of a monoclonal antibody which specifically binds to the parent polypeptide, a skilled artisan would still known how to use that polypeptide variant to make antibodies which specifically bind to the polypeptide variant. In addition, one of skill in the art would know how to use such antibodies to purify and/or detect the polypeptide variant. Therefore, the claimed antibodies meet the enablement requirement of 35 U.S.C. § 112, first paragraph.

With respect to antibodies which specifically bind to the recited immunogenic fragments of claim 11, the Examiner states that "there are no working examples demonstrating such antibody as recited in claim 11 ever been made" (Office Action, February 11, 2003; page 15). In addition, the Examiner states that "[t]here are no working examples in the specification demonstrating such antibody as recited in claim 11 ever been made (Office Action, February 11, 2003; page 17). By these statements, it appears that the Examiner would require an actual reduction to practice of the claimed invention in order to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. However, an actual reduction to practice is not necessary.

There is no statutory requirement that an invention actually be reduced to practice in order for that invention to be patentable. The amino acid sequence of the polypeptide of SEQ ID NO:1 has been explicitly disclosed in the specification (see, e.g., the Sequence Listing and Figures 1A, 1B, 1C,

1D, and 2). Methods of making and using antibodies which specifically bind to polypeptides (including polypeptides based on the SEQ ID NO:1 polypeptide) have also been disclosed in the specification (e.g., at page 28, line 6 to page 29, line 23; and page 51, line 4 to page 52, line 2). In conjunction with the disclosure in the specification and the knowledge in the art at the time the application was filed, a skilled artisan would know how to make and use the claimed antibodies. Thus, the constructive reduction to practice of the claimed antibodies more than adequately provides enablement for the claimed invention.

The Examiner asserts, with respect to chimeric antibodies, that "[i]n the absence of in vivo working examples, it is unpredictable for the following reasons: (1) the antibody may be inactivated before producing an effect, i.e. such as inherently short half-life of the antibody; (2) the antibody may not reach the target area; and (3) other function properties, known or unknown, may make the antibody unsuitable for *in vivo* therapeutic use" (Office Action, February 11, 2003; page 15). Methods to treat patients (i.e., "*in vivo* therapeutic use") with the recited chimeric antibodies are not recited in the claims. The claims at issue recite chimeric antibodies which specifically bind to polypeptides of SEQ ID NO:1. The recited chimeric antibodies can be used, for example, to detect and/or purify polypeptides which are specifically bound by the recited antibodies. Therefore, the claimed chimeric antibodies are fully enabled, and no guidance "for *in vivo* therapeutic use" is necessary.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Contrary to the standard set forth in *Marzocchi*, the Examiner has failed to provide any **reasons** why one would doubt that the guidance provided by the present specification would enable one to make and use the claimed antibodies which specifically bind to the recited polypeptides, variants, and fragments of SEQ ID NO:1. Hence, a *prima facie* case for non-enablement has not been established with respect to the claimed antibodies which specifically bind to the recited polypeptides, variants, and fragments of SEQ ID NO:1.

For at least the above reasons, reversal of this rejection is requested.

Issue 7 – Whether claims 11, 31, 32, 34, 36-43, and 58 meet the written description requirement of 35 U.S.C. § 112, first paragraph

Claims 11, 31, 32, 34, 36-43, and 58 stand rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the specification does not describe the subject matter in such a way as to reasonably convey to one of skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that "[g]iven the lack of a written description of any additional 'variants' and 'fragment' of the polypeptide of SEQ ID NO:1 to which the claimed antibodies bind, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus" (Office Action, February 11, 2003; pages 20-21). This rejection is traversed.

The Examiner assails the use of the term "comprising" by stating that "the term 'comprising' is open-ended. It expands the fragment to include additional amino acids at either or both ends. There is inadequate written description about the undisclosed amino acids at either or both ends of the fragment, much less about the epitope to which the antibody binds" (Office Action, February 11, 2003; page 19). To the contrary, the specification provides an adequate written description of antibodies which specifically bind to the recited polypeptides "comprising" SEQ ID NO:1, variants of SEQ ID NO:1, and fragments of SEQ ID NO:1.

The Examiner's assertions seem to imply that the use of the transitional phrase "comprising" in claim 11 requires that the specification provide a written description of any possible element which

could be a part of, but is not essential to, the claimed subject matter. However, the transitional phrase " '[c]omprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." M.P.E.P. § 2111.03 (citing *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997)). The specification has described numerous examples of polypeptides "comprising" the recited polypeptides, variants, and fragments of SEQ ID NO:1, such as fusion proteins and coupled proteins (Specification, e.g., at page 7, lines 24-29; page 19, lines 26-28; page 26, lines 2-15; page 28, lines 25-27; and page 51, lines 13-19). One of skill in the art would understand that Appellants had possession of the described polypeptides, "comprising" the recited polypeptides, variants, and fragments of SEQ ID NO:1, without an explicit disclosure of every possible element which could be a part of, but is not essential to, the claimed subject matter.

Moreover, the claims recite antibodies which specifically bind to epitopes on the recited polypeptides, variants, and fragments of SEQ ID NO:1. For example, the claimed antibodies specifically bind to "an epitope of a polypeptide of SEQ ID NO:1," "an epitope of a polypeptide at least 90% identical to SEQ ID NO:1," and "an epitope of the fragment [of SEQ ID NO:1]." Since the claimed antibodies specifically bind to the recited epitopes, and since there is an adequate written description of the recited polypeptides, variants, and fragments of SEQ ID NO:1, any additional amino acid residues at "either or both ends" of the recited polypeptides, variants and fragments of SEQ ID NO:1 are not essential to the claimed subject matter. Therefore, it is irrelevant whether there is an adequate written description of additional amino acid residues at "either or both ends" of the recited polypeptides, variants, and fragments of SEQ ID NO:1.

The Examiner further asserts that "there is insufficient written description about the structure such as the specific amino acid sequence of the 'epitope' or the antigenic determinant of the fragment, or the 'epitope' of a polypeptide of SEQ ID NO:1, or the 'epitope' of a polypeptide at least 90% identical to SEQ ID NO:1 to which the antibody binds" (Office Action, February 11, 2003; page 19). To the contrary. Claim 11, for example, recites antibodies which specifically bind to "an epitope of a polypeptide of SEQ ID NO:1," "an epitope of a polypeptide at least 90% identical to SEQ ID NO:1,"

and "an epitope of the fragment [of SEQ ID NO:1]." One of ordinary skill in the art would recognize polypeptide sequences which are possible epitopes of SEQ ID NO:1. The amino acid sequence of SEQ ID NO:1 provides the necessary framework for the recited epitopes - to recite every possible epitope would needlessly clutter the application. It would be routine for one of skill in the art to determine whether any possible epitope had immunogenic activity, based on the methods recited in the specification at, for example, page 8, lines 15-18; page 28, line 6 to page 30, line 1; and page 51, lines 4-19. Accordingly, the specification provides an adequate written description of the claimed antibodies which specifically bind to the recited epitopes.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*
> *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. [footnotes omitted]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

A. The specification provides an adequate written description of the claimed antibodies which specifically bind to the recited "variants" and "fragments" of SEQ ID NO:1.

The subject matter encompassed by claims 11, 31, 32, 34, 36-43, and 58 is either disclosed by the specification or is conventional or well known to one skilled in the art.

First note that the "variant" language of independent claim 11 recites polypeptides "comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, wherein said polypeptide has CoA dehydrogenase activity." Furthermore, the "fragment" language of independent claim 11 recites polypeptides "comprising an immunogenic fragment of a polypeptide consisting of the amino acid sequence of SEQ ID NO:1, wherein said fragment comprises at least 15 contiguous amino acid residues of SEQ ID NO:1." The polypeptide sequence of SEQ ID NO:1 is explicitly disclosed in the specification. See, for example, the Sequence Listing and Figures 1A, 1B, 1C, 1D, and 2. Variants of SEQ ID NO:1 are described in the specification at, for example, page 3, lines 5-6; page 6, line 18 to page 7, line 4; page 7, lines 9-12; page 14, lines 12-19; and page 15, lines 15-18; and fragments of SEQ ID NO:1 are described at, for example, page 3, lines 2-4; page 7, lines 5-9; page 8, lines 15-18; page 28, lines 21-25; and page 51, lines 7-16. In addition, a specific assay to measure CoA dehydrogenase activity is disclosed in the specification at, for example, page 50, line 21 to page 51, line 2.

One of ordinary skill in the art would recognize polypeptide sequences which are variants that are at least 90% identical to SEQ ID NO:1. Given any naturally occurring polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:1. It would also be routine to determine whether such a variant had CoA dehydrogenase activity, using the disclosed CoA dehydrogenase assay. Accordingly, the specification provides an adequate written description of the claimed antibodies which specifically bind to the recited polypeptide variants of SEQ ID NO:1.

One of ordinary skill in the art would recognize polypeptide sequences which are fragments of SEQ ID NO:1. The amino acid sequence of SEQ ID NO:1 provides the necessary framework for the recited fragments - to recite every possible fragment would needlessly clutter the application. It would be routine for one of skill in the art to determine whether any particular fragment of SEQ ID NO:1 had

immunogenic activity, based on the methods recited in the specification at, for example, page 8, lines 15-18; page 28, line 6 to page 30, line 1; and page 51, lines 4-19. Accordingly, the specification provides an adequate written description of the claimed antibodies which specifically bind to the recited polypeptide fragments of SEQ ID NO:1.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. § 112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polypeptides bound by the claimed antibodies in terms of chemical structure, rather than functional characteristics. For example, the language of independent claim 11 (as amended by the Amendment After Final filed herewith) recites chemical structure to define the claimed genus:

> 11. An isolated antibody selected from the group consisting of:
> a) an antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1, wherein the antibody specifically binds to an epitope of a polypeptide of SEQ ID NO:1,
> b) an antibody which specifically binds to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, wherein said polypeptide has CoA dehydrogenase activity, and wherein the antibody specifically binds to an epitope of a polypeptide at least 90% identical to SEQ ID NO:1, and
> c) an antibody which specifically binds to a polypeptide comprising an immunogenic fragment of a polypeptide consisting of the amino acid sequence of SEQ ID NO:1, wherein said fragment comprises at least 15 contiguous amino acid residues of SEQ ID NO:1, and wherein the antibody specifically binds to an epitope of the fragment.

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1. In the present case, there is no reliance merely on a description of functional characteristics of the polypeptides specifically bound by the claimed antibodies. The polypeptides defined by the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base the written description inquiry "on whatever is now claimed," the Examiner failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

The Patent Office Guidelines indicate that evidence that Appellants were in possession of the claimed invention can include "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, **or** some combination of such characteristics" (P.T.O. Guidelines, *supra*; emphasis added). The claimed antibodies which specifically bind the recited variants and fragments of the SEQ ID NO:1 polypeptide have been described by chemical structure (e.g., relation of the recited polypeptide variants and fragments to SEQ ID NO:1), physical properties (e.g., occurrence in nature of the recited polypeptide variants), and chemical properties (e.g., possession of CoA dehydrogenase activity by the recited polypeptide variants; specific binding of the claimed antibodies to the recited polypeptide variants and fragments). Therefore, the written description requirement has been met.

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that, rather than being a large variable genus, the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA, 1998, 95:6073-6078). Through exhaustive

analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues (Brenner et al., pages 6073 and 6076). Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins (Brenner et al., page 6076).

The present application is directed, *inter alia*, to antibodies which specifically bind to polypeptides which are short-chain dehydrogenases, including polypeptides which are short-chain dehydrogenases related to the amino acid sequence of SEQ ID NO:1. In accordance with Brenner et al., naturally occurring molecules may exist which could be characterized as short-chain dehydrogenases and which have as little as 30% identity over at least 150 residues to SEQ ID NO:1. The "variant language" of the present claims recites a polypeptide comprising "a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" (note that SEQ ID NO:1 has 313 amino acid residues). This variation is far less than that of all potential short-chain dehydrogenases related to SEQ ID NO:1, i.e., those short-chain dehydrogenases having as little as 30% identity over at least 150 residues to SEQ ID NO:1.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. § 112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those cases was based on the state of the art at essentially the "dark ages" of recombinant DNA technology.

The present application has a priority date of February 5, 1998. Much has happened in the development of recombinant DNA technology in the 20 or so years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of

polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed antibodies which specifically bind the recited polypeptide variants and fragments at the time of filing of this application.

4. Summary

The Examiner failed to base the written description inquiry "on whatever is now claimed." Consequently, the Examiner did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polypeptides recited by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Examiner.

For at least the reasons set forth above, the specification provides an adequate written description of the claimed antibodies which specifically bind to the recited polypeptide "variants" and "fragments," and this rejection should be overturned.

(9) CONCLUSION

The anticipation rejections, obviousness rejections, enablement rejections, and written description rejections should be reversed, based on at least the arguments presented above.

Due to the urgency of this matter, and its economic and public health implications, an expedited review of this appeal is earnestly solicited.

If the USPTO determines that any additional fees are due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**.

This brief is enclosed in triplicate.

Respectfully submitted,

INCYTE CORPORATION

Date: June 30, 2003.

Terence P. Lo, Ph.D.
Limited Recognition (37 C.F.R. § 10.9(b)) attached
Direct Dial Telephone: (650) 621-8581

Customer No.: 27904
3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886